

**REMARKS**

The Office Action dated September 15, 2006, has been fully considered. The present Amendment is intended to be a complete response thereto and to place the case in condition for allowance.

Claims 1-93 are pending. Claims 6-10, 16-22, and 24-93 have been withdrawn as being drawn to a non-elected invention. Claim 1 has been amended. Support for the amendment is found, *inter alia*, in the specification on page 7, lines 4-5.

**THE SPECIFICATION IS PROPER**

The specification stands objected to for the use of improperly demarcated trademarks. Applicant has amended the specification to properly demarcate trademarks and requests withdrawal of the objection.

The specification stands objected to as failing to provide proper antecedent basis for the claimed subject matter. The Examiner alleges that the protein array recited in claim 5 lacks antecedent basis in the specification because “the specification does not describe an immunoassay that is, or comprises the use of a protein array.” Applicant respectfully submits that a protein array is well known in the art, and one skilled in the art would know how to practice the present invention using a protein array without further description. For example, protein arrays are disclosed in U.S. Patent Nos. 6,406,921, 6,537,749, and 6,197,599, in detail, including how to make and use a protein array. Therefore, because one skilled in the art knows what a protein array is and how to make and use it in accordance with the present invention, the specification is proper and requires no further description of the protein array.

In addition, the Examiner alleges that “the step of comparing the levels of MIF in the serum of the individual to the MIF levels of prostate cancer patients” in claim 23 lacks antecedent basis in the specification. Applicant respectfully points the Examiner to Example 2 where MIF levels of patients with no prostate pathology, BPH, and HGPIN are compared to those with prostate cancer. This example provides proper support for claim 23.

Because the specification provides proper antecedent basis for the claimed elements, the specification is proper. Accordingly, Applicant respectfully requests withdrawal of the objection.

#### THE CLAIMS ARE PROPER

Claims 1-5, 11-15, and 23 stand objected to “as being drawn to the subject matter of non-elected inventions (i.e., the inventions of Groups III and IV), which are not linked by the linking claim.” Applicant has removed “prognosticating” from the claims. Therefore, the claims are now proper; and the objection should be withdrawn.

#### THE CLAIMS ARE NOT INDEFINITE

Claims 1-5, 11-15, and 23 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. The Examiner alleges that “claim 1 fails to recite a positive correlation step that clearly relates back to the objective of the invention.” Claim 1 has been amended to recite that “serum MIF levels of greater than about 5 to about 10 ng/ml indicates the presence of prostate cancer.” Therefore, the claim now contains a correlation step that relates to the objective of the invention. Accordingly, Applicant respectfully requests withdrawal of the rejection.

## THE CLAIMS ARE NOT ANTICIPATED

Claims 1-3 and 11-13 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Zhang et al. (*Hepatobilizry Pancreat. Dis. Int.* 2002 Nov., 1(4):577-580). Claims 1-3 and 11-15 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Mitamura et al. (*Br. J. Ophthalmol.* 2000, 84:636-639). Claims 1, 2, 4, and 11-13 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Leech et al. (*Arthritis Rheumatol.* 2000 Apr., 43(4):827-833). Claims 1-3, 11-15, and 23 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Meyer-Seigler et al. (*Cancer* 2002 Mar. 1, 94(5):1449-1456). Applicant respectfully traverses the rejections.

With regard to Meyer-Seigler et al., Applicant notes that the authors of the reference are Katherine L. Meyer-Siegler, Michael A. Bellino, and Myron Tannenbaum, and that the reference is published less than one year before the earliest priority date of the present invention. Of these authors, Mr. Bellino and Dr. Tannenbaum are not inventors of the present invention. Applicant files herewith a Declaration under 37 C.F.R. § 1.132 by Katherine L. Meyer-Siegler to show that Mr. Bellini and Dr. Tannenbaum are not inventors of the present invention because they do not contribute to the conception of any of the claimed invention. Therefore, because the Meyer-Sigler et al. reference describes Applicant's own work and is published less than a year prior to the filing date of the present application, the reference is not prior art under 35 U.S.C. § 102(a). Accordingly, withdrawal of the rejection is respectfully requested.

With regard to Zhang et al., Mitamura et al., and Leech et al., to anticipate a claim under 35 U.S.C. § 102, the reference must teach every element of the claim. See MPEP § 2131. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil*

*Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). “The identical invention must be shown in as complete detail as is contained in the ... claim.” *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim, but this is not an *ipsissimis verbis* test, i.e., identity of terminology is not required. *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990).

Neither Zhang et al., Mitamura et al., nor Leech et al. disclose every element of the claimed invention. In particular, none of the references disclose a method for detecting or diagnosing prostate cancer. Zhang et al. discloses MIF in patients with chronic virus hepatitis B and hepatitis cirrhosis. Mitamura et al. discloses MIF in the vitreous of patients with proliferative diabetic retinopathy. Leech et al. discloses the regulation of MIF in rat adjuvant-induced arthritis. Although these are unfortunate diseases, they have no relation to prostate cancer, nor has the Examiner linked any of these diseases to prostate cancer. The present invention is drawn to a method of detecting or diagnosing prostate cancer. This is not disclosed in either Zhang et al., Mitamura et al., or Leech et al. Therefore, these references cannot anticipate the present invention under the meaning of 35 U.S.C. § 102. Accordingly, Applicant respectfully requests withdrawal of the rejections.

#### THE CLAIMS ARE NOT OBVIOUS

Claims 1, 2, and 4 stand rejected under 35 U.S.C. § 103(a) as being obvious over Mitamura et al. in view of Leech et al. Claims 1, 2, and 5 stand rejected under 35 U.S.C. § 103(a) as being obvious over Mitamura et al. in view of Wright et al. (*Prostate Cancer Prostatic Dis.* 1999 Dec., 2(5/6):264-276). Claims 1-4, 11-13, and 23 stand rejected under 35 U.S.C. § 103(a) as being obvious over Hudson et al. (U.S. Patent No. 6,043,044) in view of Koong et al.

(*Cancer Res.* 2000 Feb. 15, 60:883-887) and Meyer-Siegler (*J. Interferon Cytokine Res.* 2000, 20:769-778). Applicant respectfully traverses the rejection.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *See* MPEP 2143.

With regard to Mitamura et al. in view of Leech et al., both references, as discussed above, fail to disclose a method for detecting or diagnosing prostate cancer. Their combination still does not cure this deficiency. Therefore, because Mitamura et al. in view of Leech et al. does not teach or suggest all the claim limitations, the references cannot render the present invention obvious within the meaning of 35 U.S.C. § 103.

With regard to Mitamura et al. in view of Wright et al., the deficiency of Mitamura et al. is disclosed above. The Examiner relies on Wright to teach “measuring the levels of serum biomarkers using a protein array.” However, because this teaching does not cure the deficiency of Mitamura et al., combining the references still fails to teach or suggest all the claim limitations, namely a method to detect or diagnose prostate cancer.

With regard to Hudson et al. in view of Koong et al. and Meyer-Siegler (2000), the references, taken alone or in combination, fail to teach or suggest all the claim limitations. In particular, the references fail to teach or suggest that “serum MIF levels of greater than about 5 to about 10 ng/ml indicates the presence of prostate cancer” as recited in claim 1.

Hudson et al. teach detection of prostate cancer by measuring MIF in the prostate tissue. Meyer-Siegler (2000) disclose that prostate cells secrete MIF in cell culture, not *in vitro*. Koong et al. disclose that PAI-1 is over expressed in cancer cells and is detectable in blood serum. From this information, the Examiner alleges that the present invention would have been obvious to one of ordinary skill in the art. Particularly, the Examiner alleges Koong et al. teach that “a tumor antigen, such as MIF, is over expressed and secreted by cancer cells, its presence in the serum of subject’s [*sic*] afflicted by the disease is readily determined.” This allegation is erroneous. Koong et al. merely teach that PAI-1 is detectable in blood serum. With regard to MIF, Koong et al. merely disclose that it is one of the hypoxia induced genes, but fail to mention or perform detection of MIF in the serum. Of the nine genes mentioned (*PAI-1*, *IGFBP-3*, *LRP*, *BIK*, *MIF*, *MMP-13*, *FGF-3*, *GADD45*, and *VEGF*), only the translation product of *PAI-1* was detected in the serum by Koong et al. None of the other proteins are mentioned as being found in the serum. Therefore, from this disclosure, the Examiner’s general conclusion that a secreted cancer antigen can be found in the serum is erroneous and cannot be found in the teaching of Koong et al.

Moreover, although Siegler et al. (2000) discloses the secretion of MIF by prostate cells culture, there is no teaching that these cells secrete MIF *in vivo*. The cell culture was grown and maintained in an artificial environment to induce secretion of MIF. This artificial environment does not approximate or mimic actual prostate cell condition *in vivo*. Therefore, the extrapolation of these artificial conditions to actual *in vivo* conditions is tenuous at best. Additionally, even if Siegler et al. (2000) show that the prostate cells is like to secrete MIF *in vivo*, which Applicant disputes, there is no reasonable expectation that the secreted MIF will show up in the serum. There are a multitude of biological processes that may prevent MIF from

showing up in the serum, which include being taken up by other cells or being degraded before ever reaching the serum.

In fact, Hudson et al. teach against measuring MIF in the serum because it is also expressed in the brain, eye lenses, fibroblasts, testes, and pituitary. See column 1, lines 48-56. Thus, even if secreted MIF is detectable in the serum, how does one know if it comes from the prostate or any one of the other organs and cells? Importantly, Applicant has discovered that serum MIF levels of greater than about 5 to about 10 ng/ml indicates the presence of prostate cancer. This is not disclosed by Hudson et al., Koong et al., and Meyer-Siegler (2000), taken individually or in combination. This cut off level is not obvious from the teaching of the prior art as other cells and organs may be responsible for the secretion of MIF. Hudson et al. fail to mention any specific MIF level to distinguish normal from diseased state. Neither Koong et al. nor Meyer-Siegler et al. disclose detection or diagnosis of prostate cancer and fail to mention the blood serum level of MIF that indicates a diseased state. Therefore, because the cited references fail to disclose every element of the claimed invention, they cannot render the present invention obvious.

For the reasons noted above, the present invention is not obvious over Hudson et al., Koong et al., and Meyer-Siegler (2000). Accordingly, Applicant respectfully requests withdrawal of the rejection.

## CONCLUSION

Applicant has responded to the Office Action mailed September 15, 2006. A Declaration under 37 C.F.R. § 1.132 is filed herewith. All pending claims are now believed to be allowable and favorable action is respectfully requested.

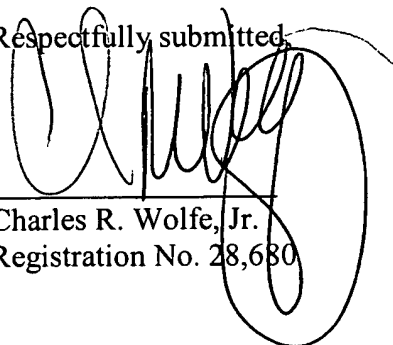
In the event that there are any questions relating to this Amendment or to the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that the prosecution of this application may be expedited.

Please charge any shortage or credit any overpayment of fees to BLANK ROME LLP, Deposit Account No. 23-2185 (111828-00109). In the event that a petition for an extension of time is required to be submitted herewith and in the event that a separate petition does not accompany this response, Applicant hereby petitions under 37 C.F.R. 1.136(a) for an extension of time.

Any fees due are authorized above.

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Respectfully submitted,



Charles R. Wolfe, Jr.  
Registration No. 28,680

BLANK ROME LLP  
Watergate  
600 New Hampshire Avenue NW  
Washington, DC 20037  
Telephone: (202) 772-5800  
Facsimile: (202) 772-5858